

the brain *de jure* is of principal interest for psychiatry.

The RDoC's target constructs, believed to reflect simple, natural-kind like behavioral functions and instantiated in circumscribed neural networks (previously called "modules"), will in all likelihood fall short from becoming an exhaustive or even a relevant *explanans* of the disorders of rationality, worldview, symbolization, self-awareness, and personal identity, which are the hallmarks of the most serious psychiatric disorders. Would clinically typical schizophrenic and bipolar patients suffer from *the same mental disorder* (i.e. share *the same* future "precision diagnosis") if they exhibit identical profiles of neurobiological and neuropsychological dysfunctions?

The justification for launching the RDoC was a failure to translate the advances of basic neuroscience into actionable psychiatric knowledge. This failure has been ascribed to the (DSM-IV) phenotype-based classification: with the passage of time, the diagnostic categories became "reified", i.e., they came to be dogmatically considered as "true" and valid entities, monopolizing research, and preventing scientists to ask novel questions, outside the DSM prescribed space (7). Yet it is also quite possible, and in my view, even likely, that the lack of progress is less related to the existence of phenotype-based classifications as such but more importantly linked to the concrete nature of DSM-III+ operational classifications.

The "operational revolution" entailed a behaviorist, subjectivity-averse stance and oversimplified psychopathology to a lay level, depriving it of

any conceptual or phenomenological framework, and resulted in inadequate or deformed phenotypic distinctions. The "operational" criteria are in fact not "operational" in any theoretically significant sense (8). Rather, the diagnoses, based on "symptom counting" and neglecting the prototypical-gestaltic structures of mental disorders, *necessarily* resulted in meaningless comorbidity, arbitrary diagnostic thresholds and hindered dimensional considerations.

The effects of "operational" simplification may be easily illustrated. An essentially *experiential-felt* origin of the schizophrenic delusion has been systematically ignored by all successive DSM/ICD definitions; perhaps because delusion cannot be grasped through a commonsensical lay definition, but always requires an embeddedness in a more overarching phenomenological framework (8). Hallucination is another example: what is called auditory verbal hallucinations is phenomenologically (qualitatively) so markedly heterogeneous (9) that treating those hallucinations as a homogeneous phenotype is likely bound to undermine empirical research. In other words, empirical research is crucially dependent on the adequacy of the employed phenotypic distinctions, adequacy that cannot be achieved through a simplistic behaviorist checklist approach.

The RDoC is legitimate as a *neuroscientific research program*, but it is hazardous as a "grand design", a totalizingly *prescriptive paradigm* for psychiatry. Reification, i.e. confusing a *concept* or idea for a really existing *thing*, deplored in the context of DSM-IV (7), will in all

likelihood repeat itself with the RDoC, yet this time with perhaps even more serious consequences. We risk what Jaspers anticipated as "psychiatry without psyche". Psychiatry will survive as a therapeutic activity because the patients will not vanish. However, psychiatry that neglects its psychopathological foundations, i.e. an interdisciplinary, theoretical and empirical study of subjectivity, risks disappearing as an academic medical discipline (10).

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# RDoC is necessary, but very oversold

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The past half century has witnessed heroic advances in the basic sciences of brain research, genetics, and molecular

biology. But there has also been a surprising and disappointing paradox: none of the exciting scientific findings has had any impact whatever on the everyday practice of clinical psychiatry. Fortunately, we have available effective treatments for most mental disorders,

but there have been no real breakthroughs in our understanding of psychopathology and ways of treating it.

Why the gaping disconnect between a basic science enterprise that is remarkably dynamic and a clinical practice that is relatively static? In fact, psy-

chiatry is really not that different from the rest of medicine in this regard. All the medical specialties have faced (and so far have largely failed to negotiate) a similar bottleneck in translational research. It turns out to be lots easier to discover the fascinating secrets of bodily functioning than to turn these to any great clinical advantage.

And because the brain is so much more complicated than other organs, psychiatry confronts by far the most challenging of all translational leaps. Our three pound brains manage to contain more neurons than there are stars in a galaxy, each connected to a thousand others and firing a thousand times a second, and with hundreds of proteins mediating the busy traffic at 100 trillion synapses. It is amazing that a machine with so many moving parts works as flawlessly as usually it does. By comparison, the breast is the most straightforward of organs, many orders of magnitude simpler than the brain. If, despite decades of intensive research, we are still early days in understanding breast cancer, why be surprised that we haven't yet gotten much of a handle on schizophrenia.

When we published DSM-III in 1980, the research future for psychiatry seemed bright and likely to deliver a quick payoff for our patients. We had great hopes that deep understanding and practical solutions would emerge quickly from the happy conjunction of powerful new research tools, generous funding from National Institute of Mental Health (NIMH) and drug companies, and the availability of a reasonably reliable diagnostic system that provided specific targets for study and treatment. Soon enough, the journals were filled with seemingly exciting findings on the genetics of mental illness and were decorated with pretty pictures that purported to show brain malfunctioning in the different mental disorders.

NIMH was at the center of the neuroscience enthusiasm, dubbing the 1990s the "decade of the brain" and betting the house on a narrow biological agenda to replace what previously had been a more balanced portfolio of research into not only the basic sciences,

but also into treatments and health services. In effect, NIMH turned itself into a "brain institute" rather than an "institute of mental health". Its efforts have succeeded in producing wonderful science, but have failed in helping patients. The brain has revealed the secrets of psychopathology only in frustratingly small packets, many of which do not replicate and none of which has been powerful enough to generate a diagnostic test or a treatment advance that would actually improve clinical practice.

NIMH has grown understandably frustrated by this lack of progress and rightly has decided to switch to the new RDoC research track that is described in Cuthbert's paper (1). Rather than continue to study the hopelessly heterogeneous categories of DSM mental disorders, it will instead focus its attention on much simpler dimensions of mental functioning, hoping that these will yield clearer biological answers.

Although the RDoC strategy is sound and necessary, the way it was recently announced to the public was badly muddled – misleading, poorly timed, and damaging to the credibility of both NIMH and the practice of clinical psychiatry. A provocative, widely reported press release came just three weeks before the publication of DSM-5. NIMH explicitly trashed all existing psychiatric diagnosis and instead offered RDoC as a better, biologically based, alternative approach. This unwise over-promising about the future blithely ignored the sobering lessons of the past and the glaring needs of our patients in the present. Lost in the bombast of the NIMH press release was that RDoC has absolutely nothing to offer in the present except an untested research tool. RDoC will almost certainly deliver nothing of practical import within this decade. My guess is that it will consist of a slow, steady slog of tiny steps, more characterized by frustrating blind alleys than by any great leaps forward.

Granted that descriptive psychiatry (as embodied in both DSM and ICD) has limited specificity and almost no explanatory power, the fact remains that it is currently the only helpful approach to psychiatric diagnosis and

continues to be essential and surprisingly useful in clinical practice. Take "schizophrenia" as an example. Our current construct is clearly a research nightmare: heterogeneous, overlapping with near neighbors, no uniform course or treatment response, and no clear pattern of gene or brain findings. Eventually this final common descriptive pathway – "schizophrenia" – will probably turn out to have hundreds of different causes and will require dozens of different treatments. But for now "schizophrenia" does very much inform clinical practice and RDoC has no replacement for it.

Moreover, it is a dangerous myth to assume that patients who meet criteria for "schizophrenia" suffer only from a brain disease. Contextual forces play a large role in the onset of schizophrenia and very often are the most crucial elements in its successful management. A supportive environment, a decent place to live, and therapeutically encouraged engagement with school, work, and social activities are now, and always will be, absolute essentials.

NIMH has had its attention so distracted by glorious dreams of a future research revolution that it has completely lost touch with the desperate suffering of schizophrenic patients in the present. It pays no attention to, and takes no responsibility for, the mess that is US mental health care. During the same fifty years that witnessed a basic science research revolution, the US has closed one million psychiatric hospital beds. But having provided too little care and housing in the community, we have been forced to open one million prison beds for psychiatric patients who were arrested for nuisance crimes, preventable had they received adequate community services and housing. These patients are suffering greatly not so much for lack of knowledge on how to care for them, but because of a lack of attention and inadequate resources. Patients with severe psychiatric illnesses are worse off in the United States than in other developed countries and their wholesale imprisonment is a throwback to the barbarity of two centuries ago.

Meanwhile, NIMH has sat silently on the sidelines ignoring this shameful transinstitutionalization. It should, but does not, feel a strong responsibility to improve the lives of our patients right now – in all the many concrete ways that are already available to us if only there were adequate funding for them. NIMH should advocate in Congress for patients, not just for its own research

budget. And the NIMH research budget should support a balanced portfolio across the entire spectrum – from bench to treatment and from treatment to community services.

Gambles on brain research are certainly necessary for a better future, but should not dominate so completely over current need.

## Road to nowhere

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B. Cuthbert presents a model aimed to integrating neuroscience and psychopathology, that may yield improvements in assessment and treatment outcome (1). The claim is that this approach is substantially different from those endorsed in the past decades, that were unable to produce biological tests which could be routinely used in diagnosis and treatment of mental disorders (2). There are no preliminary findings, however, to suggest that this is the case, nor clinical exemplifications of the usefulness of this model. Indeed, a number of problems emerge.

The model endorses a “blanket” approach: all possible biological and behavioral measurements are utilized, even though they may be highly redundant in nature, under the misguided assumption that nothing will be missed with such a strategy and innovative classification systems will ensue automatically. Quite to the contrary, conflicting results are likely to occur, with findings that may be difficult to interpret.

The model is clearly the reflection of an intellectual crisis in psychiatry, that can be attributed to a decline of clinical observation as the source of fundamental scientific challenges (3). As Feinstein remarked, in clinical medicine, “all the fundamental scholarly ideas come from elsewhere, and clinicians apparently have nothing important to contribute

beyond their work in applying the basic ideas” (4). Neurosciences have exported their conceptual framework into psychiatry much more than serving as an investigative tool for addressing the questions addressed by clinical practice.

Major clinical challenges are left without appropriate independent research supported by public sources. For instance, there is insufficient research on the frequent and vexing problem of loss of clinical effects during long-term antidepressant treatment, including exploration of its neurobiological correlates, despite the practical implications that research in this area would entail (5). Another example is that antidepressant drugs have become increasingly popular as first-line treatment of anxiety disorders, despite lack of any evidence to support their superiority (6). K. Rickels, the father of modern pharmacotherapy of anxiety disorders, wonders whether a specific study investigating comparative efficacy and differential responsiveness of newer antidepressant drugs versus benzodiazepines will ever be funded by a public source (7). In the same vein, an editorial in *Nature* (8) judged studies on psychological treatments “scandalously under-supported”, despite their “potential to make a substantive difference to patients”. It concluded that “many funding agencies around the world are too keen solely to support mechanistic investigations with potential long-term payoffs, and too unwilling to appreciate that part of their portfolio should be oriented

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towards identifying immediately effective psychological interventions” (8).

In 1967, A. Feinstein (9) urged clinicians to develop a “basic science” of their own – to study the clinical phenomena directly, to specify the importance of different types of clinical data, to create appropriate systems of taxonomy for classifying the information, and to develop intellectual models and pragmatic methods that would articulate the clinical process and use the results for quantified analyses. Such line of research, that is often subsumed under the rubric of clinimetrics, has been neglected (10). The fact that clinicians browsing a journal issue may no longer find any article relevant to their practice is a direct consequence of such neglect.

Exclusive reliance on diagnostic criteria has impoverished the clinical process and does not reflect the complex thinking that underlies decisions in psychiatric practice (10). Psychopathology and clinical judgment are discarded as non-scientific and obsolete methods. Yet, in their everyday practice, psychiatrists use observation, description and classification, test explanatory hypotheses, and formulate clinical decisions. In evaluating whether a patient needs admission to the hospital (or can be discharged from it), in deciding whether a patient needs treatment (and in case what type) and in planning the schedule of follow-up visits or interventions, the psychiatrist uses nothing more than the science of psychopathology and clinical judgment. The clinimet-